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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,594	HELLMAN, LARS T.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 25-28 are pending.

2. In view of the amendment filed 3/30/05, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 25-28 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B and (2) a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence, **does not** reasonably provide enablement for any polypeptide "comprising" at least any two CH3 IgE domains, and a any CH4 IgE domain, wherein said CH4 IgE is heterologous to at least one of said CH3 IgE domains, (2) any polypeptide "comprising" at least two rat CH3 IgE domains or at least two human CH3 IgE domains and any CH4 IgE domain, and (3) any polypeptide "comprising" at least any two CH3 IgE domains, and an opossum CH4 IgE domain, wherein said CH4 IgE is heterologous to at least one of said CH3 IgE domains as set forth in claims 25-28. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skilled in the art to practice the claimed invention. The specification disclosure is

insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B. The specification further discloses a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence wherein the CH2 and CH4 domains of the polypeptide stabilizes a functional conformation of the CH3 domain.

The specification does not teach how to make all polypeptide as set forth in claims 25-28 because there is insufficient guidance as to the structure of the polypeptide without the amino acid sequence. Further, the term "comprising" is open-ended. It expands the "polypeptide" to include additional amino acids at either or both ends. There is insufficient guidance as to which undisclosed amino acids are to be included and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. Given the unlimited number of polypeptide comprising any CH3 IgE domains so long the polypeptide contains at least two CH3 domains, any CH4 IgE domain in any order, there is insufficient in vivo working demonstrating that any polypeptide is effective for inducing anti-self IgE antibodies as a vaccine.

Nechansky *et al*, PTO 1449, teach that "although it was shown that Cε3 is the region exclusively involved in the interaction with FcεRI, the synthesis of a recombinant single Cε3 domain still being able to bind to FcεRI with high affinity has *never* been successful" (See page 296, col. 1, first paragraph, in particular). In fact, the specification on page 17-18 discloses that the CH2 and CH4 domains serve to promote and stabilize the immunogenic polypeptide such that the specific anti-self IgE response is induced. However, the conformational requirements such as natural folding or stability of IgE polypeptide have made it difficult to generate antibodies that recognize native IgE because the CH3 and CH4 domains within the claimed polypeptide can be any order. It is unpredictable which polypeptide comprising any CH4 IgE domain followed by any CH3 IgE domain followed by any CH3 IgE domain or a polypeptide comprising any CH3 IgE domain followed by any CH4 IgE domain followed by any CH3 IgE domain would maintain

secondary structure of the IgE Fc, in turn would induce anti-self IgE response specifically to the CH3 domain.

Further, there are more than 270 living species of non-placental mammals and placental mammals. There is insufficient guidance as to the structure of IgE sequence of all non-placental mammal and placental mammals, much less about the specific IgE domains.

Abaza *et al*, PTO 1449, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with antibody against the site (See abstract, in particular). Without the amino acid sequence, it is unpredictable which undisclosed immunogenic polypeptide would be useful as a vaccine for inducing anti-human IgE response in humans or anti-self IgE immune response in any animal.

Lederman et al, PTO 1449, teach that a single amino acid substitution in a common African allele of the CD4 molecule ablates binding of the monoclonal antibody IKT4 to said molecule.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 3/30/05 have been fully considered but are not found persuasive.

Applicants' position is that the presently claimed invention recites a polypeptide comprising at least two CH3 IgE domains and a CH4 IgE domain that is heterologous to at least one of the CH3 IgE domains, and the following analysis must be with respect to such a claim breadth. Second, the nature of the claimed invention is a polypeptide that can be used to generate an anti-self IgE response in a mammal. Given the nature of the invention, the state of the prior art and the relative skilled of those in the art must be determined with respect to chimeric polypeptide technology and the use of chimeric IgE polypeptide to elicit mammalian anti-self IgE responses. Third, the state of the prior art can be characterized as follows. The present application

is a continuation of application serial no. 09/401,636 (the '636 application). Those skilled in the art at the time the '636 application was filed understood IgE antibodies and their involvement with allergies. Since the early 1980's, IgE antibodies have been cloned from many species. For example, the Aveskogh et al. reference (Eur. J Immunol., 28:2738-2750 (1998)) discloses an alignment of IgE sequences from mouse, rat, sheep, pig, dog, horse, opossum, chimpanzee, orangutan, and human. Applicant notes that the disclosure of the Aveskol et al. reference is incorporated by reference into the disclosure of the present application. See, page 22, lines 26-27, and page 7, lines 1 8-19. Further, the state of the art with respect to chimeric polypeptides at the time Applicant filed was such that polypeptides were routinely engineered to contain whatever domains and sequences (i.e., tag sequences) were desire by a particular researcher or technician. Techniques for cloning homologs of polypeptides such as IgE also were routine, as evidenced by the number of IgE sequences presented in Applicant's specification and in publications such as the Aveskogh et al. reference. Third, the state of the prior art can be characterized ms follows. The present application is a continuation of application serial no. 09/401,636 (the '636 application). Those skilled in the art at the time the '636 application was filed understood IgE antibodies and their involvement with allergies. Since the early 1980's, IgE antibodies have been cloned from many species. For example, the Aveskogh et al. reference (Eur. J Immunol., 28:2738-2750 (1998)) discloses an alignment of IgE sequences from mouse, rat, sheep, pig, dog, horse, opossum, chimpanzee, orangutan, and human. Applicant notes that the disclosure of the Aveskol et al. reference is incorporated by reference into the disclosure of the present application. See, page 22, lines 26-27, and page 7, lines 1 8-19. Further, the state of the art with respect to chimeric polypeptides at the time Applicant filed was such that polypeptides were routinely engineered to contain whatever domains and sequences i.e. tag sequences) were desire by a particular researcher or technician. Techniques for cloning homologs of polypeptides such as IgE also were routine, as evidenced by the number of IgE sequences presented in Applicant's specification and in publications such as the Aveskogh et al. reference.

In response, the scope of claim 25 encompasses a polypeptide comprising any two CH3 IgE domains and any CH4 IgE domain wherein the CH4 IgE domain is heterologous to at least one of said CH3 domain and wherein the CH3 and CH4 domains are in any order such as CH3-CH3-CH4 or CH3-CH4-CH3 or CH4-CH3-CH3. The scope of claim 26 encompasses a polypeptide comprising any two rat CH3 IgE domains and any CH4 IgE domain wherein the CH3 and CH4 domains are in any order. The scope of claim 27 encompasses a polypeptide

comprising any two human CH3 IgE domains and any CH4 IgE domain wherein the CH3 and CH4 domains are in any order. The scope of claim 28 encompasses a polypeptide comprising any two CH3 IgE domains and an opossum CH4 IgE domain wherein the CH3 and CH4 domains are in any order.

The specification discloses the amino acid sequences of the CH2-CH3-CH4 domains of human, rat, and opossum IgE. The specification discloses various immunogenic polypeptide comprising opossum CH3-rat CH3--opossum CH4 (ORO); opossum-CH2-rat N-term CH3--opossum C-term CH4--opossum CH4 (ORO-trunc); opossum CH2-mouse CH3--opossum CH4 (OMO); opossum CH2-CH3-CH4 (000), platypus CH2-CH3-CH4 (PPP), opossum CH2-human CH3--opossum CH4 (OHO); opossum CH2-pig CH3--opossum CH4 (OPO); and opossum CH2--dog CH3--opossum CH4 (ODO). The specification discloses a conjugate to vaccinate rats can be designed to contain polypeptides having an N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH4 domain, and a C-terminal polyhistidine sequence. Alliteratively, the first opossum IgE CH2 domain can be followed by three rat IgE CH3 domains as opposed to only one rat IgE CH3 domain (page 14). The non-self IgE portion can contain an IgE sequence present in a non-placental mammal (e.g., opossum, platypus, koala, kangaroo, wallaby, and wombat).

The specification does not teach any polypeptide comprising any *two* CH3 IgE domains from any mammal or nonplacental mammal and any CH4 IgE domain from any mammal and non-placental mammal wherein the CH4 IgE domain is heterologous to at least on of said CH3 domain wherein the orientation can be CH3-CH3-CH4 or CH3-CH4-CH3 or CH4-CH3-CH3. The specification does not disclose the IgE amino acid sequences, the corresponding nucleotide sequence of any non-placental mammal (e.g. koala, kangaroo, wallaby, and wombat). The specification does not teach how to make all polypeptide as set forth in claims 25-28 because there is insufficient guidance as to the structure of the polypeptide without the amino acid sequence. Further, the term "comprising" is open-ended. It expands the "polypeptide" to include additional amino acids at either or both ends. There is insufficient guidance as to which undisclosed amino acids are to be included and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. The specification does not teach how to clone the other IgE sequence from other non-placental mammal e.g. platypus, koala, kangaroo, wallaby, wombat. There is no

guidance as to the oligonucleotide and hybridization condition to enable one of ordinary skilled in the art to clone the other IgE polypeptide from non-placental mammal e.g. platypus, koala, kangaroo, wallaby, wombat, in turn, to make any chimeric polypeptide as set forth in claims 25-28 as a vaccine for treating allergy.

The state of the art is such that the IgE sequences of any non-placental mammal (e.g. koala, kangaroo, wallaby, and wombat) have not been cloned. The Aveskogh et al. reference (Eur. J Immunol., 28:2738-2750 (1998)) discloses an alignment of IgE sequences from only mouse, rat, sheep, pig, dog, horse, opossum, chimpanzee, orangutan, and human. The Aveskogh et al. reference does not teach any IgE sequences from any non-placental mammal such as koala, kangaroo, wallaby, and wombat. The state of the prior art is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable. It is not routine to make any chimeric polypeptides for inducing anti-self IgE as a vaccine for treating allergy at the time in the invention was made without knowing the "structure" i.e. amino acid sequence of any chimeric polypeptides. Further, until the structure of the IgE domains from species such as koala, kangaroo, wallaby, wombat have been cloned, one of ordinary skilled in the art cannot make such chimeric polypeptide, much less use the claimed polypeptide for inducing self-IgE antibody response.

In response to applicant' argument that the declaration filed in the parent application '636 that a graduate student and technician in his laboratory were able to use a platypus IgE nucleic acid fragment and standard library screening techniques from echidna, the guidance with regard to the probes and hybridization conditions are required to enable one skilled in the art to screen for other IgE from non-placental mammal such as koala, kangaroo, wallaby, and wombat. Until the structure of the IgE from non-placental mammals such as koala, kangaroo, wallaby, wombat have been cloned, the specification as filed merely extends an invitation to one skilled in the art to come up with the claimed polypeptide having any CH3 or CH4 domains in any order from any non-placental mammals such as platypus, koala, kangaroo, wallaby, wombat. With regard to the argument that Nissim et al combined IgE domains from mouse and human to make several chimeric IgE polypeptides that were used to evaluate the regions of IgE involved in receptor binding, the scope of the claimed polypeptide is not limited to human and mouse IgE, but any two IgE CH3 and CH4 domains from any mammal and non-placental mammal in any combination of order.

In response to applicant's argument that the IgE sequence from mouse, rat, sheep, pig, dog, horse, opossum, chimpanzee, orangutan, and human were incorporation by reference to Aveskogh et al reference, the incorporation of essential material in the specification by reference to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

In response to applicant's argument that the specification provides working examples that clearly enable of the present claims, the specification exemplifies polypeptide designated ORORO and 6his-ORRRORO-his (example 7 on pages 26-27). This ORORO polypeptide contains two rat CH3 domains, two opossum CH2 domains, and one opossum CH4 domain in the following order opossum CH2, rat CH3, opossum CH2, rat CH3, and opossum CH4. However, the scope of the claims encompasses any chimeric polypeptide comprising any two CH3 and CH4 domain from any species in any order but ORORO polypeptide contains two rat CH3 domains, two opossum CH2 domains, and one opossum CH4 domain in the following order opossum CH2, rat CH3, opossum CH2, rat CH3, and opossum CH4.

In response to applicant's argument that the present specification provides multiples examples of amino acid sequences that can be added to the CH3 and CH4 IgE domains such as (signal sequence and/or a Histidine tag), the signal sequence or histidine tag is not recited in the claims. The term "comprising" expands the claimed polypeptide to include additional amino acids at either or both ends of two CH3 domains CH4 domains to include the whole IgE instead of just two CH3 domains and a CH4 domain or CH1 and CH2 domains. The specification clearly does not teach the immunogenic polypeptide comprising CH1 domain, for example.

5. Claims 25-28 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *all* polypeptide as set forth in claims 25-28 wherein the CH3 and CH4 domains are in any order for inducing anti-self IgE response in any mammal.

The specification discloses only a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B. The specification further discloses a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence wherein the CH2 and CH4 domains of the polypeptide stabilizes a functional conformation of the CH3 domain.

Other than the specific polypeptide mentioned above, there is inadequate written description about the structure associated with function of all polypeptide without the amino acid sequence. Further, the term "comprising" is open-ended. It expands the "polypeptide" to include additional amino acids at either or both ends. There is insufficient written description about the amino acids are to be added and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. Adequate written description requires more than a mere statement that it is part of the invention. The amino acid sequence itself is required. The specification provides neither a representative number of polypeptide to describe the claimed genus, nor does it provides a description of structural features that are common to all IgE CH3 domains and all IgE CH4 domains. Without the amino acid sequence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed polypeptide look like.

The specification discloses only polypeptide consisting of IgE CH2-CH3-CH4 domains from opossum, rat, human, and mouse, one of skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to describe the genus for the claimed polypeptide. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 3/30/05 have been fully considered but are not found persuasive.

Applicants' position is that Claims 25-28 recite polypeptides containing at least two CH3 IgE domains and a CH4 IgE domain, wherein the CH4 IgE domain is heterologous to at least one of the CH3 IgE domains. Applicant's specification adequately describes the claimed polypeptides. For example, the term "IgE" used throughout the specification and in the claims is a descriptive term that not only discriminates IgE polypeptides from all other polypeptides but also discriminates IgE polypeptides from IgA, IgD, IgM, and IgG polypeptide. IgE polypeptides were well known at the time Applicant filed. In fact, IgE sequences from human, rat, mouse, pig, sheep, horse, dog, chimpanzee, orangutan, and opossum were known as evidenced by Applicant's specification and the Aveskogh et al. reference. Figures 1 and 2 of applicant's specification provide the primary amino acid structures of a plurality of IgE polypeptides. For examples these figures set forth the amino acid sequences of CH3 and CH4 IgE domains from human, rat mouse, pig, and dog, opossum and platypus. In fact, Figure 2 provides an alignment of the primary amino acid structure of opossum and platypus IgE, thereby describing common structural attributes between opossum and platypus IgE. These disclosed structural attributes are representative of the genus of non-placental mammalian IgE sequences as evidenced by the fact that the structure of platypus IgE is such that a nucleic acid fragment of platypus 1gE was used to obtain an IgE sequence from another non-placental mammal, echidna via standard library screening techniques based on hybridization. See, e.g., Dr. Hellman's declaration. Given the disclosure of these IgE sequences, a person having ordinary skilled in the art would have appreciated that Applicant adequately described a representative number of species to demonstrate compliance of the written description requirement. In addition, Applicant's specification at page 26, lines 19-29 describes the structure of ORORO and 6his-ORRRORO-6his polypeptides. Given that Applicant's specification at page 15, lines 11-12 discloses that rat IgE domains of the disclosed polypeptides can be replaced with human IgE domains, Applicant's specification also describes OHOHO and 6his-OHHHOHO-6his polypeptides. In contrast to the specification at issue in the Lilly case, Applicant's specification provides a plurality of examples of amino acid sequences that could be included in the claimed polypeptides, or could be used to obtain amino acid sequences from other species for inclusion in the claimed polypeptides. Applicant also notes that in the Rochester case, the patent at issue claimed a method of achieving a biological effect, but disclosed no compounds that could accomplish that effect, and thus the

patent was deemed invalid for lack of written description. Again, in contrast to the Rochester case, Applicant's specification discloses multiple examples of amino acid sequences that can lye included in the claimed polypeptides, and also discloses multiple examples of chimeric polypeptides containing at least two CH3 IgE domains and at least one heterologous CH4 IgE domain. Thus, the holdings of the cited cases do not alter the fact that the present claims are adequately described by Applicant's specification.

In response, the scope of claim 25 encompasses a polypeptide comprising any two CH3 IgE domains and any CH4 IgE domain wherein the CH4 IgE domain is heterologous to at least one of said CH3 domain and wherein the CH3 and CH4 domains are in any order such as CH3-CH3-CH4 or CH3-CH4-CH3 or CH4-CH3-CH3. The scope of claim 26 encompasses a polypeptide comprising any two rat CH3 IgE domains and any CH4 IgE domain wherein the CH3 and CH4 domains are in any order. The scope of claim 27 encompasses a polypeptide comprising any two human CH3 IgE domains and any CH4 IgE domain wherein the CH3 and CH4 domains are in any order. The scope of claim 28 encompasses a polypeptide comprising any two CH3 IgE domains and an opossum CH4 IgE domain wherein the CH3 and CH4 domains are in any order.

The specification discloses the amino acid sequences of the CH2-CH3-CH4 domains of human, rat, and opossum IgE. The specification discloses various immunogenic polypeptide comprising opossum CH3-rat CH3--opossum CH4 (ORO); opossum-CH2-rat N-term CH3--opossum C-term CH4--opossum CH4 (ORO-trunc); opossum CH2-mouse CH3--opossum CH4 (OMO); opossum CH2-CH3-CH4 (000), platypus CH2-CH3-CH4 (PPP), opossum CH2-human CH3--opossum CH4 (OHO); opossum CH2-pig CH3--opossum CH4 (OPO); and opossum CH2--dog CH3--opossum CH4 (ODO). The specification discloses a conjugate to vaccinate rats can be designed to contain polypeptides having an N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH4 domain, and a C-terminal polyhistidine sequence. Alliteratively, the first opossum IgE CH2 domain can be followed by three rat IgE CH3 domains as opposed to only one rat IgE CH3 domain (page 14). The non-self IgE portion can contain an IgE sequence present in a non-placental mammal (e.g., opossum, platypus, koala, kangaroo, wallaby, and wombat).

However, the specification does not teach IgE sequences from species such as koala, kangaroo, wallaby, and wombat. The specification does not teach any polypeptide comprising

any two CH3 IgE domains and any CH4 IgE domain wherein the CH4 IgE domain is heterologous to at least on of said CH3 domain wherein the CH3 and CH4 domains are in any order such as CH3-CH3-CH4 or CH3-CH4-CH3 or CH4-CH3-CH3. Although IgE sequences from human, rat, mouse, pig, sheep, horse, dog, chimpanzee, orangutan, and opossum in the specification were incorporated by reference to Aveskogh et al. reference, the incorporation of essential material in the specification by reference to a publication is improper as discussed supra. The specification exemplifies only two polypeptide designated ORORO and 6his-ORRRORO-his (example 7 on pages 26-27). This ORORO polypeptide contains two rat CH3 domains, two opossum CH2 domains, and one opossum CH4 domain in the following order opossum CH2, rat CH3, opossum CH2, rat CH3, and opossum CH4. However, the scope of the claims encompasses any chimeric polypeptide comprising any two CH3 and CH4 domain from any species in any order but ORORO, for example. There is inadequate written description about the structure of the claimed chimeric polypeptide comprising any two CH3 IgE domains from any species and any CH4 IgE domain from any species wherein the CH4 IgE domain is heterologous to at least on of said CH3 domain and wherein the CH3 and CH4 domains are in any order such as CH3-CH3-CH4 or CH3-CH4-CH3 or CH4-CH3-CH3. The term "comprising" extends the CH3 and CH4 domains to include CH1 and CH2 domains of any IgE. Clearly, this is not the teachings of the disclosure. Further, there is insufficient written description about the amino acids are to be added and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. Adequate written description requires more than a mere statement that it is part of the invention. The amino acid sequence of the chimeric polypeptide itself is required. The specification provides neither a representative number of IgE polypeptide from non-placental mammal nor the method to enable one skilled in the art to screen other IgE domains from other IgE from non-placental mammal. The specification provides no structure i.e. amino acid sequence or nucleic acid sequence of any chimeric polypeptide having any two CH3 domains and one CH4 domain wherein the CH4 domain is heterologous to at least one CH4 domain other than the specific polypeptide designated ORORO and 6his-ORRRORO-his (example 7 on pages 26-27). One of skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species of IgE polypeptides to describe the genus of claimed polypeptide comprising any two CH3 IgE domains and any CH4 IgE domain wherein the CH4 IgE domain is heterologous to at least on of said CH3 domain in any order. Thus, Applicant was not in possession of the claimed genus. *See University*

of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

9. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 10, 2005

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